

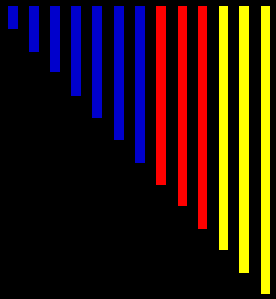

Diabetes in Children and Teens

Mary Murray, MD
Utah Diabetes Center Pediatrics
Update - 2004



Diabetes in Pediatrics

- Incidence
 - Etiology
 - Prevention
 - Treatment
-



Classification of Diabetes

- Type 1:
 - Immune mediated β -cell destruction leading to absolute insulin deficiency: most common type in children and adolescents
 - Type 2:
 - ranges from predominantly insulin resistance with relative deficiency to predominant secretory defect with insulin resistance, becoming much more prevalent in adolescents
 - Gestational diabetes
 - Other types:
 - Cystic fibrosis, drug induced, genetic syndromes
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Criteria to Diagnose Diabetes

□ Symptoms of diabetes plus random plasma glucose $\geq 200\text{mg/dl}$ (11.1 mmol/l)

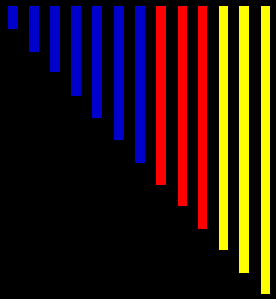
or

□ Fasting plasma glucose $\geq 126\text{ mg/dl}$ (7.0 mmol/l)

or

□ 2 hour plasma glucose $\geq 200\text{ mg/dl}$ during OGTT.

■ WHO criteria, glucose load of 1.75 gm/kg or max of 75 gm glucose in water



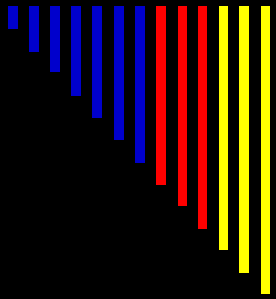
Diabetes: Incidence

- ❑ Incidence of both type 1 and type 2 is increasing world wide
- ❑ Type 1 increasing 3-5% per year worldwide
- ❑ Type 2 increasing with increasing obesity
 - ❑ Prediction that 1/3 of all Hispanic children born in 2003 will develop type 2 diabetes



Characterization of Diabetes

	Type 1	Type 2
Age	Child / Adolescent	Adolescent
Habitus	Lean	Heavy
Acanthosis	No	Yes
Family history/ Ethnicity	Uncommon (5%)/ Caucasion	Common (74-100%) / Minorities
DKA/onset	Common / rapid	Uncommon/ insidious
Insulin dependent	Lifelong	Episodic
Autoimmunity	Common (80% +)	Uncommon (70% -)



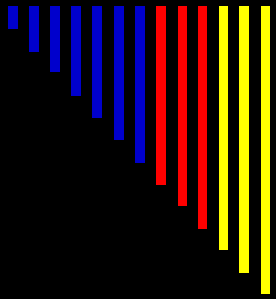
Incidence: Type 1 Diabetes

- Incidence is increasing world wide
 - In Finish children ages 0-14 years the incidence has increased from 20 per 100,000 to 50 per 100,000 over the last 40 years.
- Type 1 diabetes is still the more common type of diabetes in Caucasian children and teens
- Type 1 is not related to diet (e.g caloric intake, junk food intake)



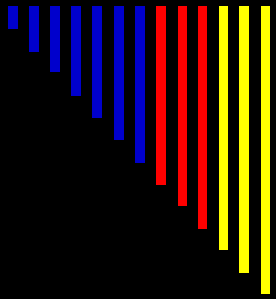
Pathophysiology of Type 1

- Type 1 Diabetes:
 - Easy to diagnose, but pathogenesis still not completely understood
 - 2 hit phenomenon:
 - Genetic predisposition
 - Second hit: infection?, environment?
 - Not preventable, not predictable
 - Evolves over weeks to months
 - Type 2 is related to lifestyle and obesity
 - Becoming more common in children especially in some ethnic groups
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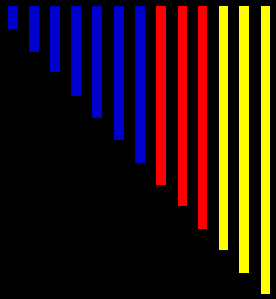
General Information

- Type 1 diabetes is the most common chronic disease of childhood
- Good control of diabetes will decrease the risk of long term complications
 - Most recent information suggests that complication rate has been cut in half in the last 20 years—and we can do better
 - Longer more productive, healthy lives
 - Must invest in the future health of our kids
- Good control must be balanced with:
 - Risk of hypoglycemia
 - Participation in all age appropriate activities



Epidemiology of Type 1

- **INCIDENCE:** 15/100,000 American children per year
 - 1M children in PCMC catchments area, 150 new cases per year (we actually have more)
- **PREVALENCE:** 1/400 by the age of 15 yrs.
 - Estimate 2500 in PCMC casement
- Peak occurrence at ages 5-7 and at puberty
- Incidence is increasing with the most marked increase in ages < 5 years



Genetic Susceptibility

- Increased risk to first degree relatives
 - Risk increases 10 fold, to 5-10%
 - Risk greater if father has diabetes
- HLA type
 - HLA-D3/4 increased risk in Caucasians
 - DQA1*0301, DQB1*0302, DQA1*0501, DQB1*0201 loci confer increased risk in Caucasians
 - Different types may be associated with different age at presentation and course



Autoimmunity

□ DAISY

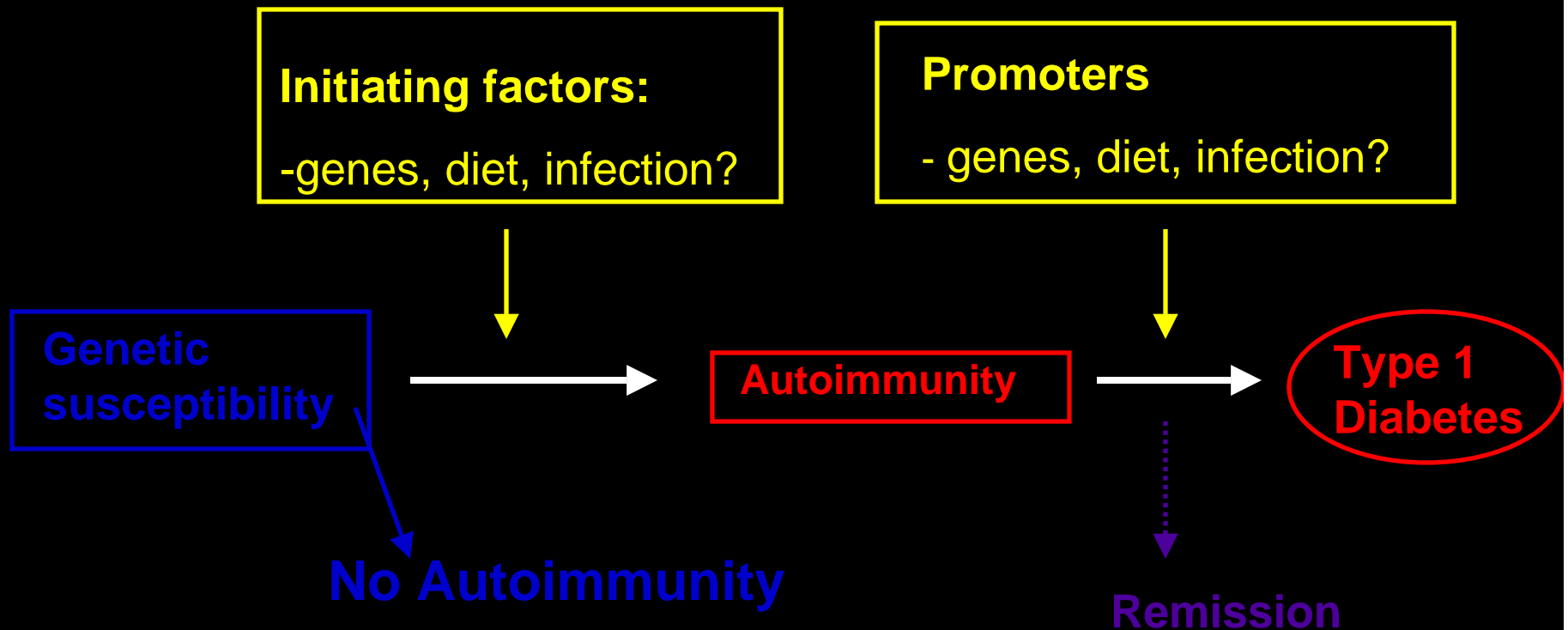
- One or more antibodies present in 85-90% at time of diagnosis
- Autoimmunity may develop at very young age and precede development of diabetes by years
- Antibody titers may vary over time

□ Antibodies associated with type 1 DM

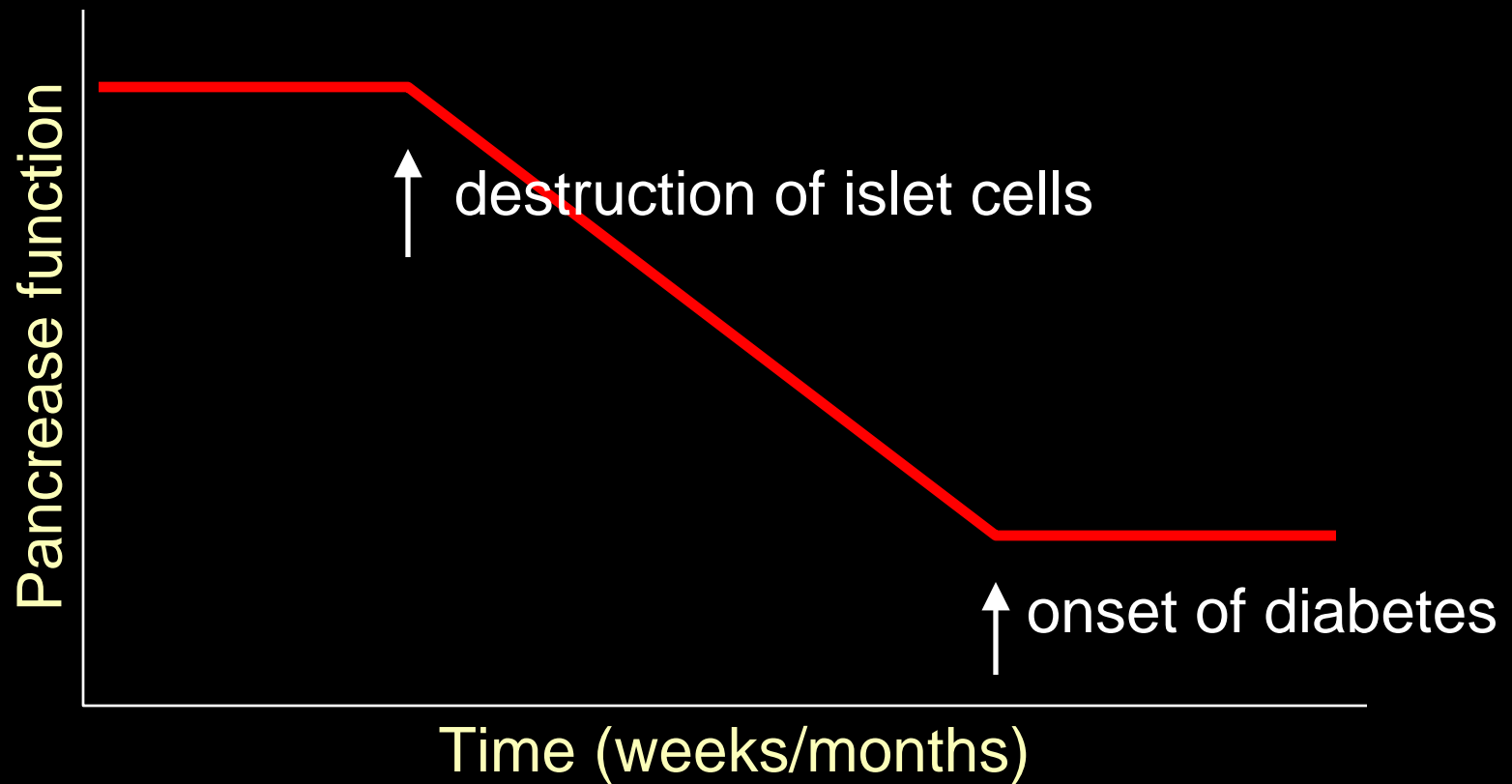
- GAD (glutamic acid decarboxylase)
 - IAA (insulin autoantibody)
 - ICA512 (tyrosine phosphatase)
-



Steps Leading to Type 1



Onset of Diabetes





Metabolic Effects of Insulin

**Peripheral
glucose utilization**



CHO Intolerance

**Hepatic
gluconeogenesis**



Fasting hyperglycemia

Lipolysis

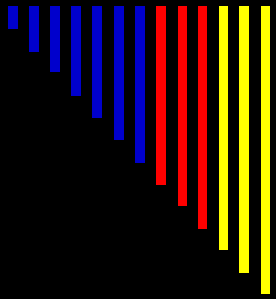


Ketosis



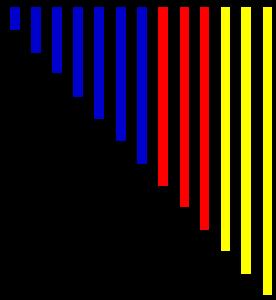
DKA

- State of absolute or relative insulin deficiency resulting in hyperglycemia and metabolic acidosis
 - Hyperglycemia - glucose >300 mg/dl
 - Acidosis - pH < 7.3
 - Incidence is decreasing in new diagnosis
 - Mortality is real, probably less than 1% in experienced hands, not always predictable
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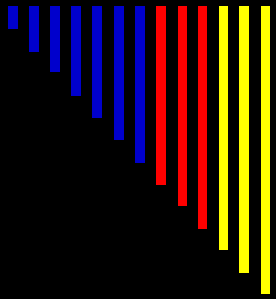
Etiology of DKA

- Hormonally mediated factors:
 - Insulin deficiency results in catabolic state
 - Counterregulatory hormone excess which accelerates catabolism
 - glucagon, cortisol, catecholamines, GH
 - Neither is sufficient
- Incidence: presenting event for 30-40% of new onset diabetes
 - Probably actually less with education
- Morbidity: 65% of all pediatric diabetic admissions



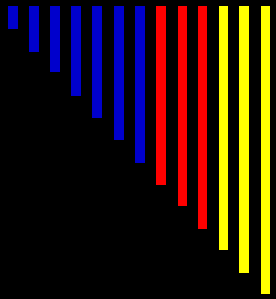
Treatment of DKA

- Standardized protocols
 - Careful fluid resuscitation – age appropriate volumes
 - Insulin infusion – IV drip at 0.1 units/kg/hr
 - Frequent blood glucose and electrolyte monitoring
- Attention to complications
 - Cerebral edema, hypocalcemia, hypokalemia



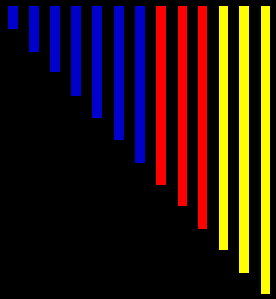
Summary

- Most children do very well and recover in 12 - 24 hours, but it is potentially fatal
- There is no substitute for close monitoring of child and labs; use ICU if there is any question or very young child
- Family needs to know severity of illness
 - Severe DKA should never happen again with appropriate home care



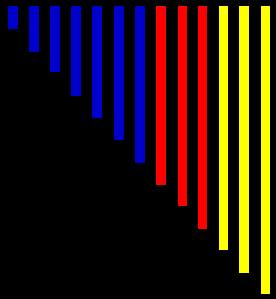
New Diagnosis

- Inpatient education program at PCMC
 - Accomplish education of family in 3 days
 - Pathophysiology and etiology
 - Insulin dosing, insulin injections, and meal planning
 - Treatment of emergencies
- Outpatient phone contact every 1-2 days over the first 2-4 weeks
- Office visit to continue education at 2-4 weeks
 - Sick days and blood ketone testing, correction dosing, trend and pattern analysis



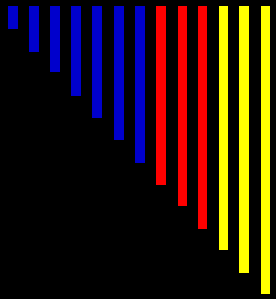
Goals of Pediatric Care

- Enable children/teens to participate in all age appropriate activities with their peers
- Risk:Benefit Ratio of Control
 - Maintain good to excellent control of diabetes
 - Minimize the episodes of hypoglycemia



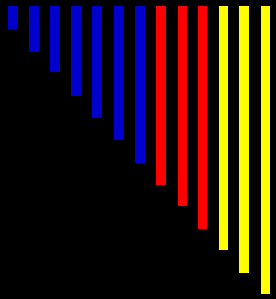
Type 1 Diabetes: Treatment

- Replacement of insulin
 - Must be administered by injection
 - Must be coordinated with food intake
- There is little usual routine anymore
 - Used to be 3 injections/day
 - Now at least 3 injections and may be as many as 7
 - Goal is to individualize therapy so as to minimize the intrusion into life



Changes in Approach

- Intensify control
 - DCCT results and impact upon long term complications
 - Increase monitoring
 - Lunch time testing
 - More frequent testing
 - Testing at different times
 - Increase insulin injections
 - Increase flexibility
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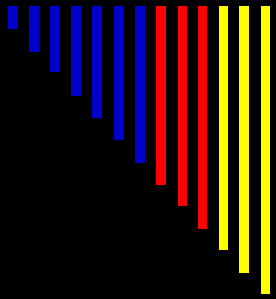
Intensive Regimens

- Multiple dosing regimens
- Generally means more testing and more shots
 - Can be done safely even in young children
 - Must use age appropriate targets and adjust for individuals, prevent hypoglycemia
- Increases flexibility



Types of Insulin

- Long acting:
 - Glargine
 - Ultralente
 - Intermediate acting:
 - NPH
 - Lente
 - Short acting:
 - Humalog™, Novalog™
 - Regular
 - Premixed:
 - 70/30, 75/25
-



Designer Insulins

- Humalog® (Lilly, LysPro insulin) and Novalog® (NovoNordisc,
 - Rapid onset, short duration
 - Match with food intake
- Lantus® (Aventis, Glargine)
 - Longer acting, no significant peak
 - Works for about 80-90% of people
 - Multiple different uses in peds

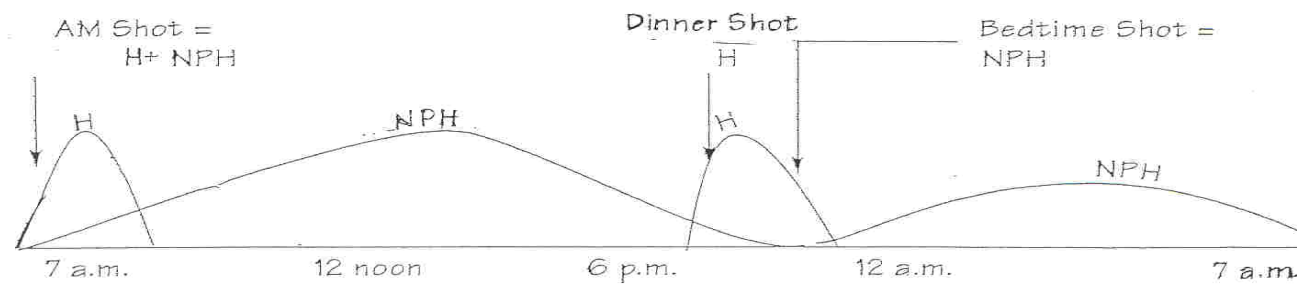


Insulin Administration

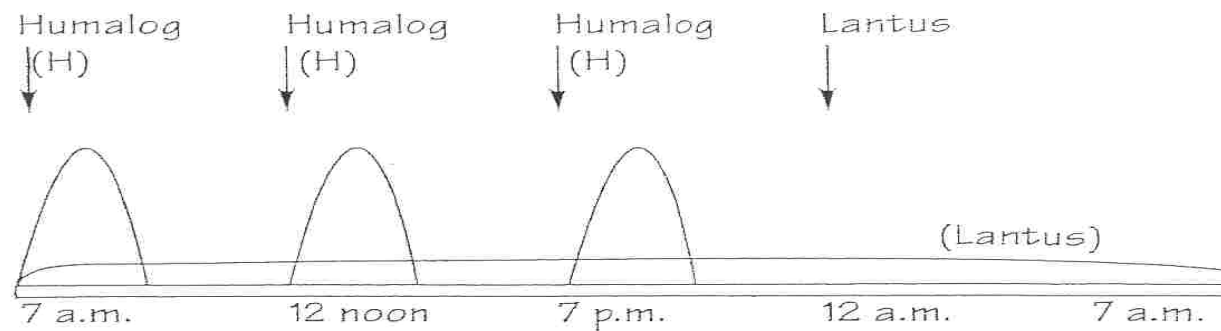
- Insulin must be coordinated with food
- Dose will vary with blood glucose level, food intake, and exercise
- Traditionally, use of NPH eliminated routine administration of lunchtime shot
 - More frequent use of pumps and lantus insulin means more children need a lunch shot of insulin
 - Lunch shots require calculation of insulin dose
 - Cover carbohydrate content and correct “out of range” blood glucose

Insulin Dosing

Humalog/Novolog + NPH Regimen



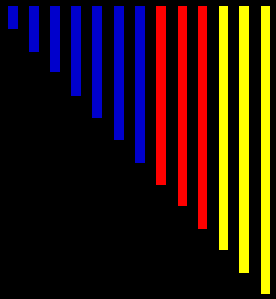
Humalog/Novolog + Lantus





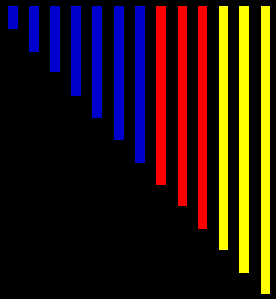
Insulin Dosing with NPH

- Mixed dosing of intermediate and short acting
 - TID dosing: mix of long and short acting
 - Mixed dose before breakfast, short acting before supper and long acting at hs
 - Requires lunch be consistent with respect to time and amount of carbohydrate
 - Lunch injections prn hyperglycemia
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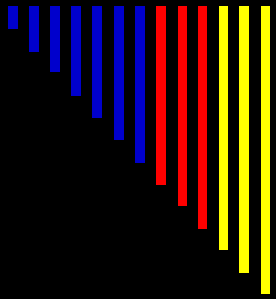
Meal Schedule on NPH

- 3 meals and 2-3 snacks
 - Mid-morning snack in young children
 - Requires structure and consistent carbohydrate intake
- Blood sugar checks
 - Before meals
 - Before bedtime snack
 - PRN



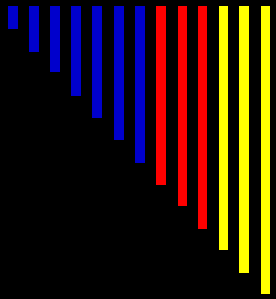
NPH Example

- Assume a 30 kg 8 year old
- Meals
 - Breakfast and lunch 60 grams of carbs, dinner 45 grams, afternoon and bedtime snack of 30 grams
- Insulin
 - Breakfast: 15 units NPH and 5 units novalog
 - Dinner: 1 unit of novalog per 15 grams of carbs
 - Bedtime: 8 units NPH
 - Correction for high glucose: 1 unit of novalog per 50 mg/dl over 150



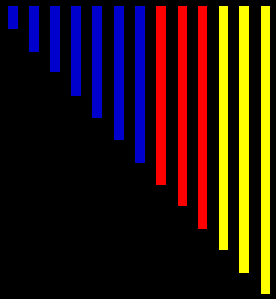
Insulin Dosing: Lantus®

- Lantus provides 20-24 hour background or basal coverage
- Additional insulin given at times of food intake
 - Meals and snacks
 - Dose for carbohydrate intake and correction of high glucose
- Increased injections provide increased flexibility
 - Both schedule and intake of food



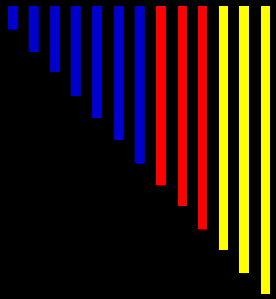
Lantus Example

- Assume a 60 kg adolescent
- Meals: ad lib
 - But must be able to calculate carb content
- Insulin:
 - Lantus, 30 units sc q hs (9-10 PM)
 - Novalog = carb dose + correction at all meals and snacks
 - Carb dose: 1 unit of novalog per 10 grams of carbs
 - Correction dose: 1 unit of novalog per 25 mg/dl over 120 (no more often than q 3 hours)



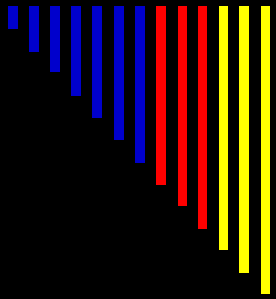
Insulin Dosing: Pump

- More intensive management than NPH
 - More flexibility
 - Similar to Lantus insulin
- CSII or insulin pump
 - Continuous sc infusion of short acting insulin
 - Requires calculation of both a carbohydrate dose for food and correction dose
- In event of pump malfunction, have only 3-4 hours of insulin coverage



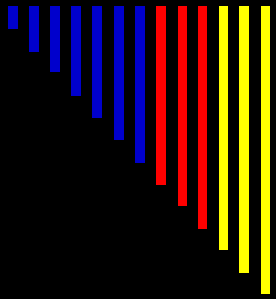
Blood Glucose

- Target range varies with age:
 - 100-200 mg/dl if age < 7
 - 80-180 mg/dl in 7-12 yo
 - 70-180 age > 12 years
- Target range is individualized
 - Modify based upon child's maturity and ability to recognize hypoglycemia (low blood sugar)
- Even in the best of all worlds, no one can achieve target range 100% of the time



Getting Control

- Blood sugar checks 4-6 times/day
 - Before meals, before bedtime and prn
- Written records
- Regular review of numbers
 - Contact with Diabetes office
 - Insulin dose changes usually no more than 1-2 times/week
- Control is not achieved instantaneously



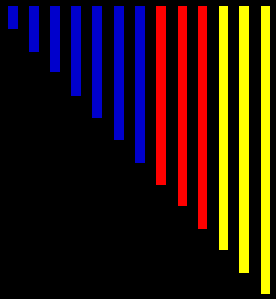
Intensify Control

□ Increase monitoring

- Meters: smaller blood volume and faster results
- Computer downloading at home
- Non-invasive monitors
 - Trends not absolutes, still requires fingerpokes

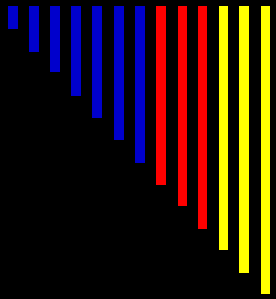
□ Flexibility

- Increase the number of injections
 - New insulins
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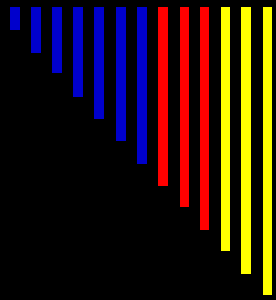
Post Prandial Blood Sugars

- Increased awareness of role of Post-prandial blood sugars in elevating HgbA₁C
- Target of the DCCT: <180 mg/dl
 - Age dependent targets
 - Age <5 yo: <200 mg/dl
 - Age 5-11 yo: <180 mg/dl
 - Age 12-18 yo: < 150 mg/dl
 - Test 1-2 hours after eating



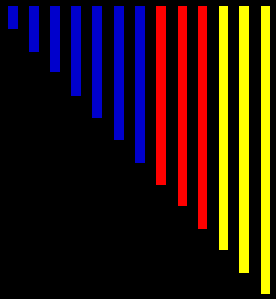
Long Term Management

- Blood glucose checks at least 4 times a day every day
 - Occasional post meal and overnight checks
- Insulin injections 3-6 times per day, every day
 - Dose calculated for blood glucose and food intake
- Quarterly office appointment
 - Hgb A₁C, review of blood glucose records
- Regular educational updates from CDE re: blood glucose management, meal planning
- Complication screening as adolescents
 - Renal, Eye, Lipid, Neurologic



Hypoglycemia

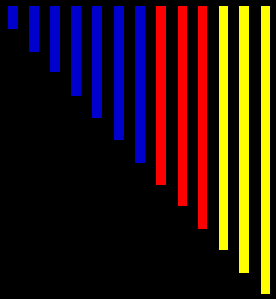
- ☐ Exercise
- ☐ Driving
- ☐ Alternate site testing



Hypoglycemia:

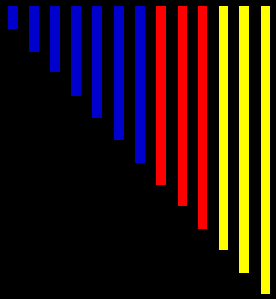
Blood sugar < 50

- Alert, able to cooperate and take po
 - 15-15 rule: 15 gms carbohydrate and recheck BS in 15 min.
 - give snack if not eating within 30 min.
 - Check on child later
 - Notify parent
- Unconscious
 - glucagon, glucose gel and call 911



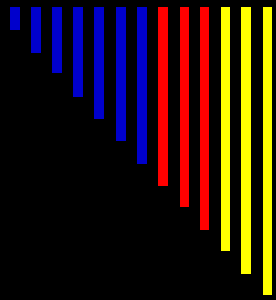
Hypoglycemia: Blood sugar 50-70

- Important not to overtreat:
 - 15-15 rule, follow with snack if not eating within 30 min.
- No one can prevent all lows.
 - Recurrent episodes may be preventable
 - Recurrent episodes may be evident as poor school performance
- Never send child out of classroom alone



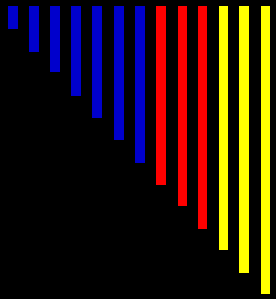
Hypoglycemia Treatment

- Low dose glucagon
 - May help prevent ER visits for mild hypoglycemia
 - Dilute glucagon and give 1 unit per year of age with insulin syringe
 - Can repeat in 20 minutes
- Severe hypoglycemic episode
 - Use standard dose of glucagon



Hyperglycemia: Blood sugar > 300

- Send home only if there are other problems, eg. vomiting
 - Check urine ketones
 - Moderate or large ketones requires more aggressive treatment, eg. additional insulin
- Hydrate with sugar free liquids
 - allow access to water and bathroom
 - prevent dehydration in hot weather
- Do not withhold food



Hyperglycemia

- Does not require leaving school
- Allow free access to water and bathroom
- Check ketones if blood sugar >300
 - If ketones large, child needs extra insulin, call parent(s) to come and get child
- Notify parent of blood sugar



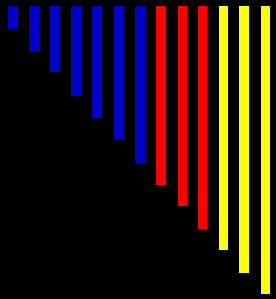
Ketones

- Blood vs urine
 - Either can be used
 - Urine is easier
 - Pitfalls of blood ketones
 - Does not equal urine testing
 - Technological difficulties, false readings
 - Only one meter, requires another type of strip and second finger poke
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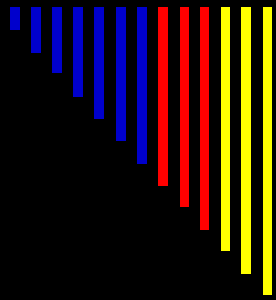
Limitations

- Avoid hypoglycemia
 - Deteriorating school performance
 - Hypoglycemia unawareness
 - Target ranges vary with age and circumstances
 - Independence
 - Insulin pens
 - Responsibility: will the child do lunch glucose and dose insulin independently? Attend to pump alarms?
 - Communication
 - Important to relay blood glucoses home; dosages are adjusted upon patterns not single values
 - Important to relay schedule changes to family for dose adjustment
-



Long Term Issues

- HgbA₁C quarterly
 - Average of blood glucose (measured and not measured)
 - Target range varies with age
 - 7.5% - 8.5%
 - Must allow for growth
- Normal growth and development
- Associated disorders
 - Thyroid and Celiac

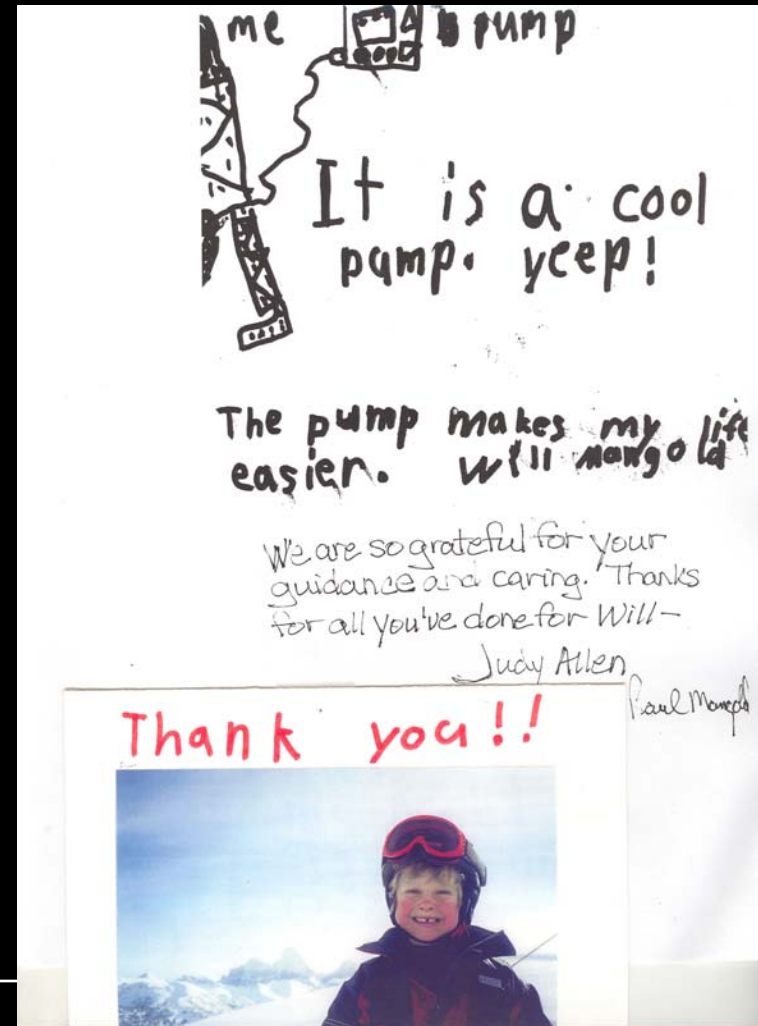


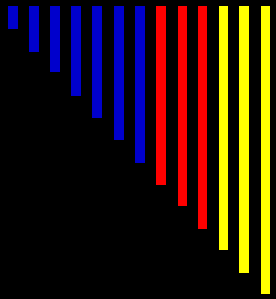
Psychological Issues

- Depression
- Needle phobias
- Eating disorders: male and female

Fitting In Diabetes

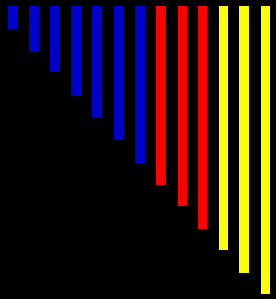
- Intensive therapy
 - Pump
 - Lantus
- Balance tight control with risk of hypoglycemia and lifestyle





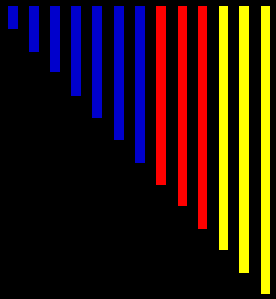
Type 1 Prevention

- Making progress to better understanding of disease etiology and development
- Need to find low risk therapy
- Need to identify at risk individuals prior to- or very early in- course of disease



Why Haven't we Prevented Type 1?

- Smoldering course
 - Hard to identify those at risk early; therefore, hard to intervene early
 - Cost of screening
- Treatment of children
 - Need interventions with excellent safety profile
 - Need accurate methods of disease prevention so as not to treat unnecessarily
- Poor understanding of immune mechanisms
 - Need better understanding of immunology
 - Redundancy of immune cascades



Diet: Cow's Milk Protein

- Early introduction of cow's milk protein
 - Ongoing study in Europe (TRIGGER)
 - DAISY: no correlation between cow's milk exposure and diabetes (JAMA, 2003)
 - BABYDIAB: no association with cow's milk (JAMA, 2003)
- Currently no evidence to implicate cow's milk exposure in development of type 1 DM



Diet: Cereals

□ BABYDIAB:

- Gluten exposure age <3 months: hazard ratio of 4 (CI=1.4-11.5; n= 4 positive children)
- No increase risk with exposure age >6mo.
- No increase risk of celiac disease associated antibodies
- All positives had high risk HLA allele

□ DAISY:

- Cereal exposure age <3 months: hazard ratio of 4.3 (CI= 2-9.3)
- Cereal exposure age > 7 months: hazard ratio 5.5 (CI= 2-13.8)
- Adjusting for HLA, family history, etc. ratio of 5.5 and 12.5 respectively
- 34 positive and 16 developed diabetes



Infection

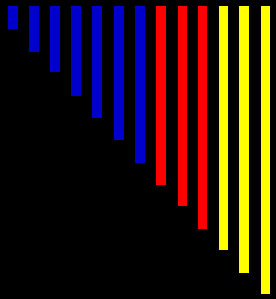
- Viral

- Enterovirus ?
- Polio
- Rubella

- Mycotoxins ?

- Immunizations

- No current data to implicate immunizations
-



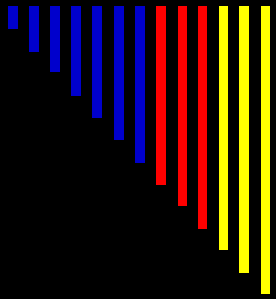
Clinical Education

- Pump preparation
 - Monthly, 12-15 families / class
- Intensive management
 - Twice a month, 4-6 families / class
- Individual education consultation
 - Weekly, 8 patients / week
- Pump Initiation
 - Weekly, 2-3 patients / week
- Medical Nutrition Consultation
 - Endocrine and Diabetes patients, weekly, 3 patients / week
- Diabetes Management in the School
 - With Pediatric Education Services at PCMC, twice a year
- Physician education programs



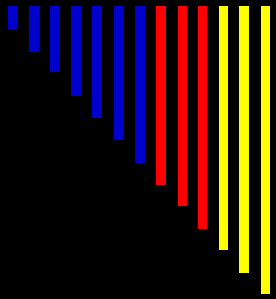
Future Programs

- Basic Carb Counting
 - Recharge your D batteries
 - For older children/teens becoming more independent, twice in summer
 - Advanced pump class
 - 6 times/year
 - Patient / Parent support groups – quarterly
 - Transitioning to independence
 - Adolescents ready to move to adult medicine program - twice a year
-



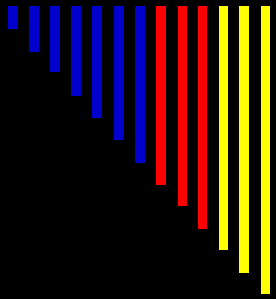
Future Technology

- Pumps and meters that communicate
 - Bolus wizard software
 - “Beam” BG to pump
- Implantable pump / BG sensor
- Non-invasive BG monitors
- Cure
 - Immune system very complex
 - Good, low risk treatment means “cure” must be have excellent risk: benefit profile



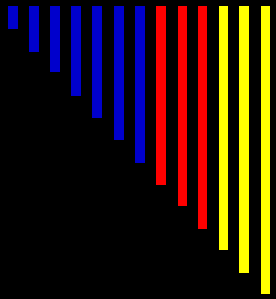
How Are We Doing?

- IHC care process model
 - Education programs for both initial and ongoing management
 - Outcome measures to be monitored through health systems database
- State Department of Health care guidelines
 - Outcome measures



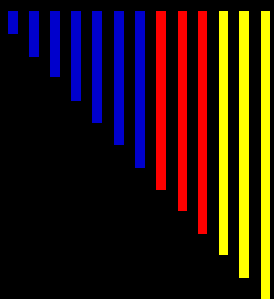
Summary

- With the exception of severe low blood sugar, children should not be sent home because of their diabetes
- Good control requires school, family, and MD participation
- If you have questions re: student's care, we will be happy to discuss problems / concerns (with parental permission)



Summary

- Control of the diabetes is individual
 - As much as you or I might want intensive management, not all children/families are able to do it
- Compromise is needed to achieve the best control possible for any one child



Questions??????